permitting specific nucleic acid hybridization". Therefore, Applicants submit that the claim as amended is definite.

2. On page 4, the Office rejected Claim 25 as being unclear due to the term complementary nucleic acid molecule. Applicants have amended Claim 25 to remove the term "complementary", and therefore submit that the amended claim is definite.

3. In Claim 31, the Office argues that the term "substantially hybridizes" is vague, and requests clarification. Applicants submit that the term "substantially hybridizes" is defined on page 9, lines 5-9 of the specification as follows:

> "The term "**substantially hybridizes**" means that two nucleic acid molecules can form an anti-parallel, double-stranded nucleic acid structure under conditions (e.g. salt and temperature) that permit hybridization of sequences that exhibit 90% sequence identity or greater with each other and exhibit this identity for at least a contiguous 50 nucleotides of the nucleic acid molecules."

4. In Claim 31, the Office argues that the term "determining" does not set forth a positive step. Applicants have replaced the term with "detecting", and therefore submit that the amended claim is definite.

5. Claim 32 has been amended to provide proper claim construction from the antecedent term "hepatocyte".

Rejections under 35 U.S.C. § 102

A. Amended Claims 31 and 32 and dependent Claim 33 are not anticipated

On page 5 of the Office Action, Claims 31-35 were rejected as being anticipated by Hillman et al. Claims 34-35 are cancelled. Applicants have amended Claims 31-32 to read on SEQ NOs: 280, 384, and 488. Claim 33 is dependent on Claim 32. Applicants further submit that Hillman *et al.* does not disclose SEQ NOs: 280, 384, and 488. Because present claims 31 and 32 as amended do not read on subject matter disclosed in Hillman *et al.*, Applicants request that the 102 (e) rejection in light of Hillman be withdrawn.

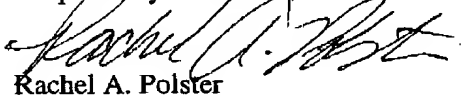
On page 5 of the Office Action, Claims 31-35 were rejected as being anticipated by Upton *et al.* Applicants have amended Claims 31-32 to read on SEQ NOs: 280, 384, and 488. Claim 33 is dependent on Claim 32. Applicants further submit that Upton *et al.* does not disclose SEQ NOs: 280, 384, and 488. Because present claims 31 and 32 as

amended do not read on subject matter disclosed in Upton *et al.*, Applicants request that the 102 (b) rejection in light of Upton be withdrawn.

On page 6 of the Office Action, Claims 31-35 were rejected as being anticipated by Lee *et al.* Applicants submit that the sequence disclosed in Lee *et al.* were not correlated with the effects of toxic compounds on gene expression and cancer progression. Rather, Lee *et al.* describes the over-expression of ESTs from PC-12 cells (from a rat pheochromocytoma cell line) in response to treatment with nerve growth factor to induce the acquisition of a neuronal phenotype, and the last paragraph on page 8307 suggests that "Application of the comparative EST approach can be readily extended to other cellular processes, such as development, homeostasis, cell-cycle regulation, apoptosis, cancer progression, and toxicological effects of drugs on gene expression." Claims 31 and 32 are directed towards the differential mRNA expression in hepatocytes in response to treatment with a compound to determine carcinogenicity. Applicants submit that Claims 31 and 32 do not read on the subject matter disclosed in Lee et al., and therefore request that the 102 (b) rejection in light of Lee *et al.* be withdrawn.

In view of the foregoing amendments and remarks, Applicants believe that all claims now active in the present application are in condition for allowance. Therefore, passage of the application and claims to issue is requested. If the Examiner has any further comments or concerns, he is welcome to contact Applicants at the number below.

Respectfully submitted,



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II. AMENDMENTS TO THE CLAIMS

Please amend the specification as follows:

Claims 1-24 (Cancelled)

Claim 25 (Currently Amended) A method for determining a level or pattern of a carcinogenesis biomarker in a cell comprising:

(a) incubating, under conditions permitting specific nucleic acid hybridization, a marker nucleic acid molecule, said marker nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ NOS: 280 and 488 or complements thereof, with a ~~complementary~~ nucleic acid molecule obtained from said cell, wherein nucleic acid hybridization between said marker nucleic acid molecule, and said complementary nucleic acid molecule obtained from said cell permits the detection of said carcinogenesis biomarker;

(b) permitting hybridization between said marker nucleic acid molecule and said complementary nucleic acid molecule obtained from said cell; and

(c) detecting the level or pattern of said complementary nucleic acid, wherein the detection of said complementary nucleic acid is predictive of the level or pattern of said carcinogenesis biomarker.

Claim 26 (Original) The method of claim 25, wherein said level is predictive of said carcinogenesis biomarker.

Claim 27 (Original) The method of claim 25, wherein said pattern is predictive of said carcinogenesis biomarker.

Claim 28 (Original) The method of claim 25, wherein said level or pattern is detected by *in situ* hybridization.

Claims 29-30 (Cancelled)

Claim 31 (Currently Amended) A method for measuring the carcinogenicity of a composition comprising:

i. culturing a cell line;

ii. exposing said cell line to said composition; and

iii. determining the presence or absence of mRNA which substantially hybridizes to at least one nucleic acid sequence selected from the group consisting of SEQ NOS: 280, ~~317~~, 384, ~~465~~, and 488 and complements thereof.

Claim 32 (Currently Amended) A method for measuring the carcinogenicity of a composition comprising:

a. exposing a ~~cell, tissue sample, or test mammal~~ hepatocyte to said composition; and

b. ~~determining~~ detecting the presence or absence in said hepatocyte ~~cell, tissue sample, or test mammal of~~ mRNA which substantially hybridizes to an at least one nucleic acid sequence selected from the group consisting of SEQ NOS: 280, ~~317~~, 384, ~~465~~, and 488 and complements thereof.

Claim 33 (Original) The method of claim 32, wherein said ~~mammal~~ hepatocyte is a rat hepatocyte.

Claims 34-35 (Cancelled)